Fig. 6. Reaction types allowing simultaneous reaction and linker cleavage.

Nucleophilic substitution using activation of electrophiles

FIG. 6A. Acylating monomer building blocks - principle

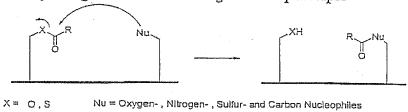


FIG. 6B. Acylation

Amide formation by reaction of amines with activated esters



FIG. 6C. Acylation

Pyrazolone formation by reaction of hydrazines with β -Ketoesters



FIG. 6D. Acylation

Isoxazolone formation by reaction of hydroxylamines with β -Ketoesters



FIG. 6E. Acylation

Pyrimidine formation by reaction of thioureas with $\beta\text{--}Ketoesters$

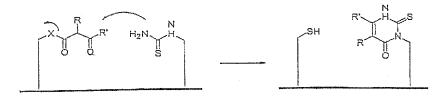


FIG. 6F. Acylation

Pyrimidine formation by reaction of ureas with Malonates

FIG. 6G. Acylation

Coumarine or quinolinon formation by a Heck reaction followed by a nucleophilic substitution

X = O.S X' = Halogen, OTI, OMs Z = O, NH

FIG. 6H. Acylation

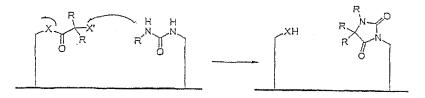
Phthalhydrazide formation by reaction of Hydrazines and Phthalimides

FIG. 6I. Acylation

Diketopiperazine formation by reaction of Amino Acid Esters

X = 0, S R' = H, R

FIG. 6J. Acylation Hydantoin formation by reaction of Urea and α-substituted Esters



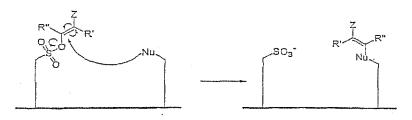
X = O, S X' = Hal, OTos, OMs, etc.

FIG. 6K. Alkylating monomer building blocks - principle Alkylated compounds by reaction of Sulfonates with Nucleofiles



Nu = Oxygen-, Nitrogen-, Sulfur- and Carbon Nucleophiles

FIG. 6L. Vinylating monomer building blocks - principle



Z = CN, COOR, COR, NO $_2$, SO $_2$ R, S(=0)R, SO $_2$ NR $_2$, F Nu = Oxygen- , Nitrogen- , Sulfur- and Carbon Nucleophiles

FIG. 6M. Heteroatom electrophiles

Disulfide formation by reaction of Pyridyl disulfide with mercaptanes



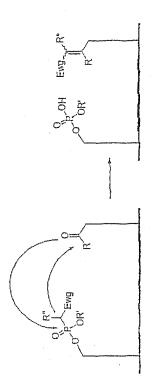
FIG. 6N. Acylation

Benzodiazepinone formation by reaction of Amino Acid Esters and Amino Ketones

x=0,s

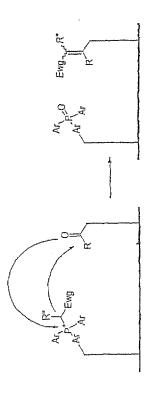
Addition to carbou-hetero multiple bonds

FIG. 60. Wittig/Horner-Wittig-Emmons reagents Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones



Ewg = CN, COOR, COR, NO2, SO2R, S(=0)R, SO2NR2, F etc.

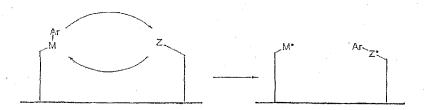
FIG. 6P. Wittig/Horner-Wittig-Emmons reagents Substituted alkene formation by reaction of Phosphonates with Aldehydes or Ketones



Ewg = CN, COOR, COR, NO2, SO₂R, S(=0)R, SO₂NR₂, F etc. Ar= aryf, helaryl

Transition metal catalysed reactions

FIG. 6Q. Transition metal cat. Arylations



Z = haloaryl, halohelaryl, ArOMs, ArOTI, ArOTos or NHR or OH or SH ele.

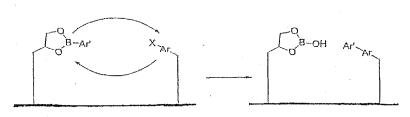
Z* = Aryl, hetaryl, NR or O or S etc

 $M = e.g. BR, BR_2^-, SnR_2 etc.$

R = H, alkyl, aryl, hetaryl, OR, NR₂

 $M^* = e.g. B(OH)R, B(OH)R_2^*, Sn(OH)R_2 etc.$

FIG. 6R. Arylation Biaryl formation by the reaction of Borates with Aryls or Heteroaryls



X = Halogen, OMs, OTf, OTos, etc

FIG. 6S. Arylation Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls

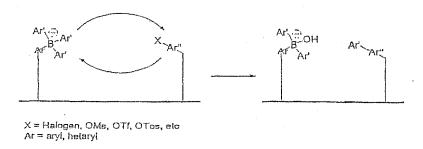


FIG. 6T. Arylation Biaryl formation by the reaction of Boronates with Aryls or Heteroaryls

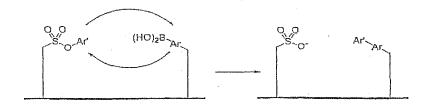


FIG. 6U. Arylation

Arylamine formation by the reaction of amines with activated Aryls or Heteroaryls

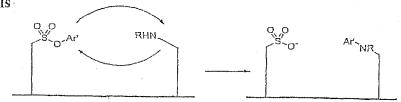


FIG. 6V. Arylation

Arylamine formation by the reaction of amines with hypervalent iodonium salts

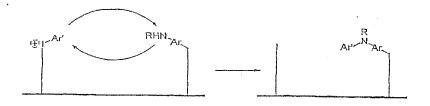
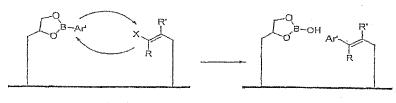


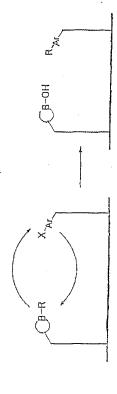
FIG. 6X. Arylation

Vinylarene formation by the reaction of alkenes with Aryls or Heteroaryls



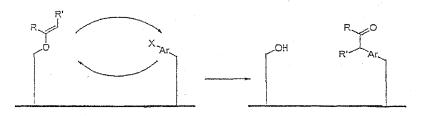
X = Halogen, OMs, OTI, OTos, etc.

FIG. 6Y. Alkylation Alkylation of arenes/hetarens by the reaction with Alkyl boronates



X = Halogen, OMs, OTf, OTus, etc

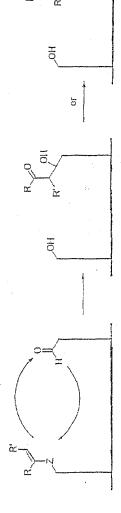
FIG. 6Z. Alkylation Alkylation of arenes/hetarenes by reaction with enolethers



X = Halogen, OMs, OTf, OTos, etc

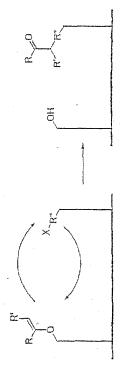
Nucleophilic substitution using activation of nucleophiles

FIG. 6AA. Condensations
Alkylation of aldehydes with enolethers or enamines



Z = NR, O; X = Halogen, OMs, OTf, OTos, etc

FIG. 6AB. Alkylation Alkylation Alkylation of aliphatic halides or tosylates with enolethers or enamines



X = Halogen, OMs, OTf, OTos, etc

Cycloadditions

FIG. 6AC. [2+4] Cycloadditions

$$R_3 \xrightarrow{R_2 \times R_1} R_3$$

$$R_4 \xrightarrow{R_5} R_4$$

$$Z \approx 0.NR$$

FIG. 6AD. [2+4] Cycloadditions

Y = CN, COOR, COR, NO2, SO2R, S(=0)R, SO2NR2, F

FIG. 6AE. [3+2] Cycloadditions

Y = CN, COOR, COR, NO₂, SO₂R, S(=0)R, SO₂NR₂, F

FIG. 6AF. [3+2] Cycloadditions

Y = CN, COOR, COH, NO₂, SO₂R, S(=O)R, SO₂NR₂, F

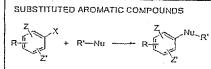
FIG. 7A. Pairs of reactive groups X,Y and the resulting bond XY.

Nucleophilic substitution reactions

RX +	R'-0	İ	R-0-R'	ETHERS	RACK + R"-NH,	0.00
R-X +	R'5"	1	R-S-R	THIOETHERS		HIUAMIDES
R-X +	R'-NH2	1	R-N-R'	sec-AMINES	R-(+ R"-NH ₂ R-(A	AMDES
 + *	R-H-H	1	R-N-R	tert-AMINES	m HM-R"	
 +	R -0	† -	HO OR'	β-HYDROXY ETHERS	$R \stackrel{+}{\leftarrow} + R' - NH_2 \stackrel{-}{\sim} - R \stackrel{+}{\sim} T$	THIOAMIDES
÷	R's'	1	HO SR.	p-HYDROXY THIOETHERS	R"-X + N OH N OH N OH	OXIMES
+	R'VH2	ţ	HI HILL	p-HYDROXY AMINES	R'-502G + R'M'R R'502-H S'	SULFONAMIDES
 # **	R. – 0,	1	KHIN OR.	p-amino Ethers	$R' - X + R - \stackrel{Z'}{\leftarrow} 1$	DI-AND TRI- FUNCTIONAL COMPOUNDS
 0 R-{ 0-R'	R"—NH2	1	R-CO	AMIDES	$R - \begin{pmatrix} 0 & + & R - \begin{pmatrix} Z \\ + & R - \begin{pmatrix} Z \\ + & Z \end{pmatrix} \end{pmatrix} $	DŁ AND TRI- FUNCTIONAL GOMPOUNDS
 R-Co+	R"—NH2	t.	R{0 HI4-R"	AMDES	$Z'.Z' = COOR, CHO, COR, CONR^2,$ $NO_2, SOR, SO_2R, SO_2NR^2,$	COO, ed.
 And the Party of t	***************************************	-	The second secon			

FIG. 7B

Aromatic nucleophilic substitution



Nu = Oxygen-, Nilrogen-, Sulfur- and Carbon Nucleophiles X = F, Cl, Br, I, OSO₂CH₃, OSO₂CF₃, OSO₂TOL, , , etc. Z'.Z = COOR, CHO, COR, CONR-2, COO", CN, NO₂, SOR, SO₂R, SO₂R, SO₂RR'2, , ect.

FIG. 7C Transition metal catalysed reactions

FIG. 7D Addition to carbon-carbon multiple bonds

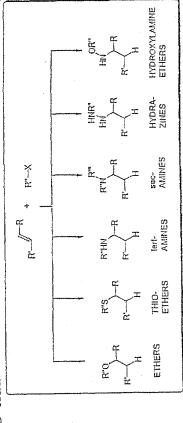


FIG. 7E

$\sum_{Z'} + \underbrace{ = Z' - \frac{Z}{Z}}_{Z'} + \underbrace{ FUNCTIONAL}_{Z'}$	Z = H, Alkyl, Ar, $Z' = Z'$, Alkyl, Ar, $Z' = COOR$, G10, COR, CONR"2, CN, NO2, SOR. SO ₂ R, SO ₂ N"2, ect.
$\begin{cases} z & T \\ + & + \\ Z' & R' \\ & R'' \\ & COMPOUNDS \\ \end{cases}$	Z = H, Alkyl, Z', Ar Z'' = COOR, CHD, COR, CONR'2, CM, NO_2 , SOR, SO ₂ R, SO ₂ NR'2 ect. Z' = Z'' R = R', = R', = Z

FIG. 7F Cycloaddition to multiple bonds

+	SUBSTITUTED CYCLOALKENES	A A A A A A A A A A A A A A A A A A A	SUBSTITUTED CYCLOALKENES
2 H H H H H H H H H H H H H H H H H H H	SUBSTITUTED CYCLODIENES	H + H H H H H H H H H H H H H H H H H H	SUBSTITUTED CYCLOALKENES
R. H. N. H. Z.	SUBSTITUTED 1,2,3-TRIAZOLES	Z = COOR, CHO, COR, COOH COAr CN, NO ₂ , Ar, CH ₂ OH, CH ₂ NH ₂ , CH ₂ CN, SOR, SO ₂ R elc. R = H, Alkyl, Ar, Z X = 0, NR, CR ₂ , S,	CN, NO ₂ , , SO ₂ R etc. CR ₂ , S,

FIG. 7G Addition to carbon-hetero multiple bonds

		<u></u>		7
Substituted Alkenes	Substituted Alkenes	SOR, Aryl)2, ect.	
R"O_B Z + 0 R + R' R + R' R''	R H H H H H H H H H H H H H H H H H H H	Z'.Z' = COOR, CHO, COR, CONR''2, CN, NO2-SOR, SO2R', SO2NR''2, ect. R" = H, Alkyl, Aryl Aryl	$Z = COOR$, CHO, COR, SOR, SO_2R , CN, NO_2 , ed. $R = R$, H, Alkyl, Ar, $R^* = R^*$, H, Alkyl, COR ,	A STATE OF THE PARTY OF THE PAR
β-Hydroxy Ketones β-Hydroxy Aldehydes	Vinyl Kelones Vinyl Aldehydes	Substituted Alkanes	R. Subsiliuled L.Z. Amines Subsiliuted AH Animes	
R H O H O	R R-	R. Z.	NH R" NABHION R	
R" H + R" H	o * x o =	z'^z + R'_R	Z + CH ₂ O + R" R-NH ₂ + CH ₂ O + R"	

Figure 8. Cleavable Linkers

FIG. 8A. Linker for the formation of Ketones, Aldehydes, Amides and Acids

FIG. 8B. Linker for the formation of Ketones, Amides and Acids

 ${\tt FIG.}\,\,$ 8C . Linker for the formation of Aldehydes and Ketones

FIG. 8D. Linker for the formation of Alcohols and Acids

FIG. 8E. Linker for the formation of Amines and Alcohols

 ${\tt FIG}$. ${\tt 8F}$. Linker for the formation of Esters, Thioesters , Amides and Alcohols

$$R = 0$$
 $R = XH$
 $R = 0H + R$
 $X = 0$, S, NHR, NR,

FIG. 8G. Linker for the formation of Sulfonamides and Alcohols

FIG. 8H. Linker for the formation of Ketones, Amines and Alcohols

FIG. 8I. Linker for the formation of Ketones, Amines, Alcohols and Mercaptanes

FIG. 8J. Linker for the formation of Biaryl and Bihetaryl

FIG. 8K. Linker for the formation of Benzyles, Amines, Audins Alcohols and Phenoles

FIG. 8L. Linker for the formation of Mercaptanes

TCER = Iris(2-carboxyethyl)phosphine

FIG. 8M. Linker for the formation of Glycosides

FIG. 8N. Linker for the formation of Aldehydes and Glyoxylamides

FIG. 80 Linker for the formation of Aldehydes, Ketones and

Descriptors of

Descriptors of CSPN 2

S

11 言意えん ニースイ

hybridizing region 1 Complementary

hybridizing region 2 Complementary

Frameshift control (may be present or absent)

IIIIII Optional descriptor for type and/or number (a.o.) of functional entities on CCPN 1

Frameshift control (may be present or absent)

RIGHT Descriptor for R-group on CCPN 2

Optional descriptor for type and/or number (a.o.) of functional entities on CCPN 2

Spacer (may be present or absent)

34/35

Figure 10

Functional Entity

Functional Entity

CCPN containing two hybridizing regions

CCPN containing one hybridizing region

Descriptor for substituent or scaffold type (a.o.) -CCPN compo-

Optional call or answer region - signalering in which context this CCPN is allowed Optional call or answer region – signalering in which context this CCPN is allowed 1

FIG. 11